REMARKS

Upon entry of this amendment, Claims 5, 7-9, 26, 27, 29, 31, 35, 37, 48-51, 56, 58, 69, 70, 72, 74, 76, 78, 107, 108, 110, 117, 127-129, 131-135, 137, 147, 150, 156, and 157 are pending in the present application. Among them, Claims 56, 110, 135, 137, 147, and 150 are directed to non-elected inventions or species, and are withdrawn from further consideration.

New Claim 157 corresponds to former canceled Claim 68.

The remaining claims are canceled without prejudice. Applicants reserve the right to prosecute claims of identical or similar scope in one or more future continuing applications.

Applicants have amended Claim 5 to clarify the subject matter claimed. Amended Claim 5 incorporates the subject matter of the previously non-elected species as claimed in formerly withdrawn Claim 47. Applicants' attorney Yu Lu contacted the Examiner on May 18, 2007 to inquire the possibility of making the above amendment upon filing an RCE. After consulting his supervisor, the Examiner replied that allowing such an amendment is generally at the discretion of the Examiner, and in the instant case, the Examiner would allow such an amendment. Applicants wish to thank the Examiner for exercising his discretion to allow the proposed claim amendment.

Applicants note that the IDS filed on Oct. 2, 2006 has been considered by the Examiner.

Applicants respectfully request reconsideration in view of the following remarks. Issues raised by the Examiner will be addressed below in the order they appear in the Office Action.

Claim Rejections under 35 U.S.C. § 112, second paragraph

Claims 1, 5, 10 and 11 remain rejected for reciting the allegedly indefinite term "potent."

While Applicants do not necessarily agree with the Examiner's arguments, solely to advance prosecution, Applicants have amend Claim 31 to replace "potent" with "active." Applicants submit that the amendment does not change the scope of the claim. Applicants have also deleted the reference to "potentcy" in Claim 5 to obviate this rejection.

Applicants note that Claims 10 and 11 are canceled, and the rejections to these claims are rendered moot.

Applicants submit that all pending claims satisfy the requirements of 35 U.S.C. § 112, second paragraph. Reconsideration and withdrawal of the rejections are respectfully requested.

Claim Rejections under 35 U.S.C. § 112, first paragraph - enablement

Claims 1, 10-17, and 33 remain rejected under 35 U.S.C. § 112, 1st paragraph, for allegedly failing to meet the enablement requirement by reciting certain kinetic properties.

Since these claims are canceled without prejudice, the rejections are rendered moot.

Claims 4 and 86 remain rejected under 35 U.S.C. § 112, 1st paragraph, for allegedly failing to meet the enablement requirement by reciting adzymes producing cleavage products that inhibits the substrate or adzyme cleavage.

Since these claims are canceled without prejudice, the rejections are rendered moot.

Claims 131 and 132 are rejected under 35 U.S.C. § 112, 1st paragraph, for allegedly failing to meet the enablement requirement. The Office Action asserts that these claims recite an adzyme composition formulated to inhibit autocatalytic by including a reversible protease inhibitor. However, the Office Action alleges that "it is not clear that there are available reversible inhibitors for any proteases nor are other means of formulating an adzyme composition to present [sic] auto proteolysis are taught." This is a new ground of rejection not raised in the previous Office Action.

Applicants respectfully disagree. There are numerous art-recognized reversible protease inhibitors, many (if not all) are commercially available. For example, **Sigma-Aldrich** sells numerous **broad-spectrum protease inhibitors**, such as Serine protease inhibitors, Cysteine protease inhibitors, Aspartic protease inhibitors, and Metalloproteinase inhibitors, including Leupeptin, Aprotinin, Pepstatin A, EDTA, *etc.* *See* http://www.sigmaaldrich.com/Area_of_Interest/Biochemicals/Enzyme_Explorer/Key_Resources/Protease_Inhibitors/Broad_Spectrum_Inhib_.html (**Exhibit A**).

Also *see* the **Santa Cruz Biotechnology, Inc.** web site http://www.scbt.com/support-table-protease_inhibitors.html, and **CALBIOCHEM** web site for properties of selected protease inhibitors www.emdbiosciences.com/html/cbc/Protease_Inhibitor_Properties.htm (**Exhibit A**).

According to these companies, **Leupeptin** reversibly inhibits trypsin-like serine proteases such as trypsin, chymotrypsin, chymase, pepsin and thrombin, it also inhibits selected

cysteine proteases such as calpain, cathepsin B, H & L and papain; **Aprotinin** is a reversible inhibitor of esterase and serine protease activity such as trypsin, chymotrypsin, kallikrein, plasmin, urokinase, and leukocyte protease; **Pepstatin A** is a reversible inhibitor of acid proteases such as pepsin, renin, chymosin, protease B and cathespin D and many microbial aspartic proteases; **EDTA** is a reversible metalloprotease inhibitor. *See* **Exhibit A.**

"A patent need not teach, and preferably omits, what is well known in the art. *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987); and *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984)." MPEP 2164.01.

The Examiner's argument seems to be directly contradictory to the evidence Applicants have provided. On the other hand, the Examiner has not provided any scientific reasoning or evidence to support his assertion. If this assertion is based on personal knowledge, Applicants respectfully invite the Examiner to provide an affidavit or declaration setting forth specific factual statements and explanation to support the finding. *See* 37 C.F.R. § 1.104(d)(2). Applicants also respectfully remind the Examiner that "[i]f applicant adequately traverses the examiner's assertion of official notice, the examiner must provide documentary evidence in the next Office action if the rejection is to be maintained. *See* 37 CFR 1.104(c)(2). *See* also *Zurko*, 258 F.3d at 1386, 59 USPQ2d at 1697 ("[T]he Board [or examiner] must point to some concrete evidence in the record in support of these findings" to satisfy the substantial evidence test)." *See* MPEP 2144.03, Section C.

In that regard, Applicants also respectfully remind the Examiner that "[a]s long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. 112 is satisfied. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Failure to disclose other methods by which the claimed invention may be made does not render a claim invalid under 35 U.S.C. 112. *Spectra-Physics, Inc. v. Coherent, Inc.*, 827 F.2d 1524, 1533, 3 USPQ2d 1737, 1743 (Fed. Cir.), *cert. denied*, 484 U.S. 954 (1987)." MPEP 2164.01(b).

Therefore, based on the teaching of the instant specification, coupled with what is well-known in the art, a person of ordinary skill in the art would be able to formulate the claimed pharmaceutical preparation to prevent autocatalysis, for example, by using a myriad of available

reversible protease inhibitors, such as those described herein.

In view of the foregoing, all pending claims satisfy the enablement requirement of 35 U.S.C. § 112, first paragraph. Reconsideration and withdrawal of the rejection are respectfully requested.

Claim Rejections under 35 U.S.C. § 102

Claims 1, 5, 7-17, 25, 35, 37, 38, 40-42, 44, 52, 66, 69, 70, 84, 91, 93, 95, 97, 107, 108, 127, and 133 remain rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Holvoet *et al.* (*JBC* 266: 19717-24, 1991, "Holvoet"). Specifically, the Office Action argues that Holvoet teaches a plasminogen activator – fibrin-specific antibody fusion protein.

Applicants submit that the amended claims are novel in view of Holvoet. Specifically, Holvoet describes a fusion protein comprising a urokinase-type plasminogen activator (uPA) and a fibrin-specific antibody. The fusion protein binds the fibrin clot via its fibrin-specific antibody, but the uPA catalytic domain does not cleave the fibrin clot. Instead, it cleaves the soluble zymogen plasminogen in the circulating blood to yield an active Ser protease plasmin, which in turn dissolves the fibrin clot. In other words, the substrate for the Holvoet enzyme is the soluble zymogen plasminogen, which is not a "biomolecule in a biomolecular accretion," as recited in the claims.

Therefore, Holvoet cannot anticipate the claimed invention.

Claims 4, 5, 7-9, 11-17, 31, 35, 37, 38, 40-44, 52, 58, 66, 69, 70, 72, 74, 76, 78, 80, 82, 84, 86, 91, 93, 95, 97, 99, 101, 107, 108, 113, 115, 117, 119, 127, 128, and 156 remain rejected for allegedly being anticipated by Davis (WO 00/64485, or "Davis").

Applicants respectfully disagree, because Davis fails to teach a "fusion protein" as recited in the claims.

Although the Examiner did not explain in this Office Action what the term "fusion protein" means, the Examiner admits, in nearly identical context in an Office Action issued in a related co-pending application U.S.S.N. 10/650,591, that "David et al. fuse a catalytic domain (like protease) to a targeting moiety via chemical cross linking agent" (emphasis added, see page 7, towards the end of the first paragraph in the July 25, 2007 Office Action in the co-pending application U.S.S.N. 10/650,591). Thus, it appears that the Examiner has apparently

misunderstood the meaning of "fusion protein" as recited in the claims. According to the Examiner's interpretation, two or more chemically cross-linked polypeptides (such as those taught in Davis) are also "fusion proteins."

Applicants assert that chemically cross-linked two or more polypeptides are not a single "fusion protein" within the scope of the claims. Thus Davis cannot anticipate the claimed invention.

Claims 4, 5, 7, 8, 11-17, 25-27, 31, 35, 37, 38, 40-44, 52, 58, 60, 66, 69, 70, 72, 74, 76, 78, 80, 82, 84, 86, 91, 93, 95, 97, 99, 101, 107, 108, 113, 115, 117, 119, 127, 128, and 156 remain rejected for allegedly being anticipated by Chen (US 2003/0068792, or "Chen").

Applicants respectfully disagree, because Chen also fails to teach a "fusion protein" as recited in the claims.

Specifically, Chen relates to a so-called "targeted enzyme" that "comprises a substrate recognition site and has been modified from a pre-targeted enzyme to comprise one or more targeting sites, each targeting site comprising one or more variant sequences, and to bind to a target with higher affinity than the corresponding pre-targeted enzyme binds the target under like conditions. ... Targeted enzymes of the invention **do not include** enzymes with a targeting site that consists of a polypeptide or other target-binding molecule that is attached to the N- or C-terminus of the pre-targeted enzyme (e.g., as in a histidine tagged protein or **a fusion protein**), a targeted enzyme whose only target is a monoclonal antibody, or a targeted enzyme made by increasing or optimizing the binding of a pre-targeted enzyme to a substrate of a reaction catalyzed by the pre-targeted enzyme" (emphasis added).

In other words, the "targeted enzyme" of Chen merely modifies so-called "variant sequences" on the pre-targeted enzyme, such that after the modification, the enzyme acquires the ability to bind a target that the enzyme previously cannot bind. In doing so, Chen explicitly states that the "targeted enzyme" **does not include** any fusion protein created by fusing a targeting domain to (the catalytic domain of) a discrete and heterologous enzyme (see emphasis above), as is recited in the claimed invention.

The above disclosure in Chen, especially the bold emphasis "targeted enzymes of the invention **do not include** ... **a fusion protein**," is directly contradictory to the Examiner's assertion that "Chen et al teach fusion proteins ..." Applicants reiterate that the targeted enzyme

in Chen is not a fusion protein with a catalytic domain fused to a "heterologous" targeting domain, because what Chen calls "catalytic polypeptide domain" and "targeting site" are from the same "pre-targeted enzyme" (see quoted passage above).

If the Examiner wishes to maintain this rejection, Applicants respectfully invite the Examiner to explain for the record why and how the Chen construct can be viewed as a "fusion protein" with "discrete and heterologous" "protease domain" and "targeting site," as recited in the claims, despite the fact that Chen explicitly denies that its construct is such a fusion protein.

Claims 1 and 10-17 are rejected for allegedly being anticipated by Chen and Holvoet.

Since these claims are canceled without prejudice, the rejection is rendered moot.

In summary, Applicants submit that Holvoet, Chen and Davis all fail to teach at least one limitation recited in the presently claimed invention, and thus none can anticipate the claimed invention. Reconsideration and withdrawal of the rejections are respectfully requested.

Claim Rejections under 35 U.S.C. § 103(a)

The Office Action rejects Claims 1, 5, 7-9, 25-27, 29, 31, 33, 35, 37, 38, 40-44, 52, 66, 69, 70, 72, 74, 76, 78, 80, 82, 84, 91, 93, 95, 97, 99, 101, 107, 108, 113, 115, 117, 119, 127-130, 133, 134, and 156 are rejected under 35 U.S.C. § 103(a) as allegedly being obvious in view of Holvoet (*supra*), Davis (*supra*), Chen (*supra*), and Guo *et al.* (*Biotec. and Biong* **70**: 456-463, 2000, or "Guo") in view of Sallberg *et al.* (U.S. Pat. No. 6,960,569) or Whitcomb (*supra*).

Specifically, the Examiner argues that Whitcomb teaches mesotrypsin, which is "fairly stable to proteolytic cleavage;" and Sallberg teaches "fusion protein of mutated NS3/4A protease domain of HCV conjugated to antibody or other protein wherein fusion protein is resistant to proteolytic cleavage (mutation of breaking point residues of protease causes resistance to the proteolytic cleavage)."

Thus, the Examiner concludes that "... it would have been obvious to one of ordinary skill in the art to use mesotrypsin – a trypsin-like protease that is fairly stable to proteolytic cleavage as taught by Whitcomb et al. or mutation of protease as taught by Sallberg and conjugate said proteases by a linker as taught by Guo *et al.* to target domain as taught by Holvoet ... or Davis ... or Chen and use the resulting adzyme to inactivate substrate polypeptides by catalyzing the proteolytic cleavage of the [sic] said substrate polypeptide."

Applicants respectfully disagree for the reasons which follow.

First of all, Applicants submit that **Davis or Chen cannot be combined with Guo, Whitcomb, or Sallberg** to arrive at a fusion protein that cleaves a biomolecule substrate that is in a biomolecular accretion, as recited in the amended claims.

As argued before (see above), neither Chen nor Davis teaches or suggests a fusion protein as recited in the claims. In fact, Applicants submit that, because both Chen and Davis explicitly teaches away from using "fusion proteins," Guo (allegedly teaching the use of a polypeptide linker for making fusion proteins), Whitcomb (allegedly teaching the use of mesotrypsin as the catalytic / protease domain), and Sallberg (allegedly teaching a protease resistant protease domain in a fusion protein) cannot be properly combined with Chen or Davis, because doing so would change the principle of operation in Chen and Davis.

Pursuant to MPEP 2143.01: "[i]f the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims *prima facie* obvious. *In re Ratti*, 270 F.2d 810, 123 USPQ 349 (C.C.P.A., 1959)." Therefore, neither Chen nor Davis can be properly combined with Guo, Whitcomb, or Sallberg.

Even if Whitcomb or Sallberg is combined with Davis or Chen, the combination results in non-fusion protein constructs that may have a mesotrypsin protease domain or NS3 protease domain. But the constructs are still not fusion proteins as required in independent Claim 5.

In view of the foregoing, a *prima facie* case of obviousness has not been established. Reconsideration and withdrawal of the rejections under 35 U.S.C. § 103(a) are respectfully requested.

Double Patenting Rejection

The Office Action states that Claims 4 and 5 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claim 2, 19, and 35 of the co-pending U.S. Application Nos. 10/792,498 and 10/650,591. Similarly, the Office Action also rejects other claims of the instant application on the ground of obviousness-type double patenting over various claims in these two co-pending U.S. applications.

Applicants submit that the double patenting rejection is rendered moot in view of the claim amendment. Specifically, the pending claims as amended recite that the "substrate is a biomolecule in a biomolecular accretion," which limitation is not present in either the 10/792,498 application claims or the 10/650,591 application claims. Thus the pending claims are patentably distinct from those of the U.S.S.N. 10/792,498 and U.S.S.N. 10/650,591.

In any event, Applicants submit that, pursuant to MPEP 804, "[i]f the 'provisional' double patenting rejection in one application is the only rejection remaining in that application, the examiner should then withdraw that rejection and permit the application to issue as a patent [without filing a terminal disclaimer], thereby converting the 'provisional' double patenting rejection in the other application(s) into a double patenting rejection at the time the one application issues as a patent." Thus, should the double patenting rejection is maintained, Applicants respectfully request the Examiner to hold the provisional double patenting rejection in abeyance until the indication of allowable subject matter in this or the other co-pending applications.

If conflicting claims are first allowed in these two co-pending U.S. Applications, and appear in an issued U.S. patent, Applicants note that, pursuant to 37 C.F.R. § 1.130(b), a timely filed terminal disclaimer in compliance with 37 C.F.R. § 1.321(c) may be used to overcome the double patenting rejection. Applicants will submit a terminal disclaimer, if necessary, upon indication of allowable subject matter.

CONCLUSION

The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. The Director is hereby authorized to charge any other deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. **18-1945**, from which the undersigned is authorized to draw under Order No. **COTH-P01-001**.

Dated: October 26, 2007

Respectfully submitted,

By_____

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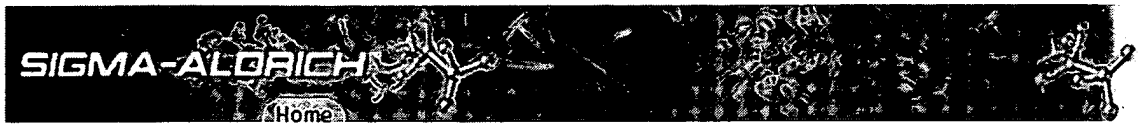

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Protein Kinase Explorer
+ Lipids
+ Peptide Explorer
+ Pharmacopoeia
+ PolyAmino Acids

Broad-Spectrum Inhibitors of Proteolytic Enzyme Classes

Enzyme Explorer

Serine Protease Inhibitors

Product Code	Inhibitor	Characteristics	Typical Working Concentration	Prep. of Stock Solutions
L2884	Leupeptin	Inhibits trypsin-like serine proteases such as trypsin, chymotrypsin, chymase, pepsin and thrombin. Inhibits selected cysteine proteases such as calpain, cathepsin B, H & L and papain.	10-100 µM	10 mM in water, stable 6 months at -20 °C
P7626	PMSF	Broad spectrum serine protease inhibitor. Also reported to inhibit some cysteine proteases such as papain.	0.1-1.0 mM	Prepare fresh in anhydrous ethanol or isopropanol at 200 mM
A8456	AEBSF	Broad spectrum serine protease inhibitor. Also reported to inhibit some cysteine proteases such as papain.	0.1-1.0 mM	100 mM in water, stable 1 month at -20 °C
A1153	Aprotinin	Does not inhibit thrombin or factor Xa.	0.3 µM or equimolar	Freely soluble in water and stable at 2-8 °C
C7268	Chymostatin	Inhibits chymotrypsin-like serine proteases such as chymase cathepsins A,B,D and G. Also inhibits some cysteine proteases such as papain.	10-100 µM	10 mM in DMSO, stable at -20 °C
A9141	Antithrombin III	Inhibits thrombin, kallikreins, plasmin, trypsin and factors Ixa, Xa, and Xia	equimolar	Soluble at 10 un/ml in water, prepare stock solutions at neutral pH store at -20 °C

+ Radiochemicals
+ Vitamins and Derivatives

D7910	3,4-Dichloroisocoumarin	Broad spectrum serine protease inhibitor	5-100 µM	10 mM in DMSO, stable at -20 °C
T7254	TLCK	Inhibits trypsin-like serine proteases	10-100 µM	Prepare fresh at 10 mM in 1 mM HCl
T4376	TPCK	Inhibits chymotrypsin-like serine proteases	10-100 µM	10 mM in ethanol, stable at 4 °C
D0879	DIFP	Highly toxic cholinesterase inhibitor. Broad spectrum serine protease inhibitor. Hydrolyzes rapidly in aqueous solutions	0.1 mM	Prepare in anhydrous isopropanol at 200 mM
A6191	Antipain	Inhibits serine proteases such as plasmin, thrombin and trypsin. Also inhibits some cysteine proteases such as calpain and papain.	1-100 µM	10 mM in water, stable 1 month at -20 °C
M6159	α2-Macroglobulin	Broad spectrum protease inhibitor	equimolar	Water soluble, stable at -20 °C

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Cysteine Protease Inhibitors

Product Code	Inhibitor	Characteristics	Typical Working Concentration	Prep. of Stock Solutions
E3876	N-Ethylmaleimide	Binds stoichiometrically to SH groups	equimolar	Water soluble at >10mg/ml, prepare fresh
L2884	Leupeptin	Inhibits trypsin-like serine proteases such as trypsin, chymotrypsin, chymase, pepsin and thrombin. Inhibits selected cysteine proteases such as calpain, cathepsin B, H & L and papain.	10-100 µM	10 mM in water, stable 6 months at -20 °C
E3121	E-64	Will not inhibit serine protease with the exception of trypsin	1-10 µM	1 mM in water, stable at -20 °C
C7268	Chymostatin	Inhibits chymotrypsin-like serine proteases such as chymase cathepsins A,B,D and G. Also inhibits some cysteine proteases such as papain	10-100 µM	10 mM in DMSO, stable at -20 °C
A6191	Antipain	Inhibits serine proteases such as plasmin, thrombin and trypsin. Also inhibits some cysteine proteases such as calpain and papain.	1-100 µM	10 mM in water, stable 1 month at -20 °C
M6159	α2-Macroglobulin	Broad spectrum protease inhibitor	equimolar	Water soluble, stable at -20 °C
		Broad spectrum serine protease		Prepare fresh in anhydrous ethanol

P7626	PMSF	inhibitor. Also reported to inhibit some cysteine proteases such as papain.	0.1-1.0 mM	or isopropanol at 200 mM

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Aspartic Protease Inhibitors

Product Code	Inhibitor	Characteristics	Typical Working Concentration	Prep. of Stock Solutions
P5318	Pepstatin A	Inhibits aspartic proteases such as renin, chymosin and pepsin	1 µM	1mM in methanol or DMSO, stable at -20 °C
M6159	α2-Macroglobulin	Broad spectrum protease inhibitor	equimolar	Water soluble, stable at -20 °C

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Metalloproteinase Inhibitors

Product Code	Inhibitor	Characteristics	Typical Working Concentration	Prep. of Stock Solutions
ED2SS	EDTA	Broad spectrum metalloproteinase inhibitor	1-10 mM	Very soluble and stable in water
P9375	1,10-Phenanthroline	Broad spectrum metalloproteinase inhibitor	1-10 mM	200mM in methanol or DMSO, stable at -20 °C
R7385	Phosphoramidon	Strong inhibitor of metalloendoproteinases, thermolysin and elastases, but a week inhibitor of collagenase	1-10 µM	1 mM in water, stable 1 month at -20 °C
B8385	Bestatin	Inhibitor of aminopeptidases	1-10 µM	1 mM in methanol, stable 1 month at -20 °C
M6159	α2-Macroglobulin	Broad spectrum protease inhibitor	equimolar	Water soluble, stable at -20 °C

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References

1. Proteolytic Enzymes: A Practical Approach, R. J. Benyon and J. S. Bond, Eds, pp. 241-249 (1994)
2. Handbook of Enzyme Inhibitors, 2nd ed, H. Zollner (1993)
3. Sigma Data

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Protease Inhibitors

PRODUCT	CATALOG #	DESCRIPTION	AMOUNT
Aprotinin	sc-3595	Reversible inhibitor of esterase and serine protease activity such as trypsin, chymotrypsin, kallikrein, plasmin, urokinase, and leukocyte protease.	50000 KIU
Calpain Inhibitor I	sc-29119	Inhibitor of Ca^{2+}-dependent neutral cysteine proteases calpain I and calpain II, papain, cathespin B and L; weak inhibitor of cathespin H and α-chymotrypsin; does not inhibit trypsin; recommended starting concentration: 17 µg/ml.	25 mg
Complete™ Protease Inhibitor Cocktail Tablet	sc-29130	Mixture of several protease inhibitors with broad inhibitory specificity; for the inhibition of serine, cysteine, and metalloproteases in bacterial, mammalian, yeast, and plant cell extracts; 1 tablet contains sufficient protease inhibitors for 50 ml cell extract.	20 tablets
Complete™ Protease Inhibitor Cocktail Tablet, EDTA-free	sc-29131	Mixture of several protease inhibitors; for the inhibition of serine, cysteine, but not metalloproteases; 1 tablet contains sufficient protease inhibitors for 50 ml cell extract.	20 tablets
Leupeptin	sc-3141	Reversible inhibitor of serine and cysteine proteases such as calpain, plasmin, trypsin, papain, and cathepsin B, no inhibition found with pepsin, cathepsins A and D, thrombin, or α-chymotrypsin; recommended starting concentration 0.5 µg/ml.	0.5 mg
Pepstatin A, synthetic	sc-45036	Reversible inhibitor of acid proteases such as pepsin, renin, chymosin, protease B and cathespin D and many microbial aspartic proteases; recommended starting concentration 0.7 µg/ml.	5 mg
Phenylmethylsulfonyl Fluoride (PMSF)	sc-3597	Inhibits serine proteases like chymotrypsin, trypsin, and thrombin and cysteine protease papain; does inhibit metalloproteases, most cysteine proteases, and aspartic proteases; recommended starting concentration: 17-170 µg/ml.	1 gram
Trypsin Inhibitor, soybean	sc-29129	Inhibits trypsin as well as factor Xa, plasmin, and plasma kallikrein; does not inhibit metallo-, cysteine, aspartic proteases, or tissue kallikrein; recommended starting concentration: 10-100 µg/ml; from soybean.	50 mg

Protease Inhibitor Cocktails
- Overview/Selection Guide
- Protease Inhibitor Cocktail Sets
- ▶ Properties of Selected Protease Inhibitors
- Frequently Asked Questions

Phosphatase Inhibitor Cocktails
- Overview/Selection Guide
- Phosphatase Inhibitor Cocktail Sets
- Selected Protein Tyrosine Phosphatase Inhibitors
- Selected Serine/Threonine Phosphatase Inhibitors

▶ Properties of Selected Protease Inhibitors

Product	Cat. No.	Target Protease Class and Mechanism of Action	Solubility	Suggested Concentration
AEBSF, Hydrochloride	101500	Water soluble, non-toxic alternative to PMSF. Irreversible inhibitor of serine proteases. Reacts covalently with a component of the active site. Inhibits chymotrypsin, kalikrein, plasmin, trypsin and related thrombolytic enzymes.	H_2O	0.1-1 mM
ALLN	208719	Inhibits calpain I (K_i = 190 nM), calpain II (K_i = 220 nM), Cathepsin B (K_i = 150 nM), and cathepsin L (K_i = 600 pM).	Methanol, Ethanol, DMSO	0.2-2 µM
Aprotinin, Bovine Lung	616370	A serine protease inhibitor that acts as a competitive and reversible inhibitor of proteolytic and esterolytic activity. In cell cultures, extends the life of cells and prevents proteolytic damage to intact cells.	H_2O	0.6-2.0 µg/ml
Aprotinin,		A serine protease inhibitor that acts as a competitive and reversible inhibitor of proteolytic and esterolytic activity. In		

Recombinant NEW!	616371	cell cultures, extends the life of cells and prevents proteolytic damage to intact cells.	H_2O	0.6-2.0 µg/ml
Bestatin	200484	Binds to cell surfaces and inhibits cell surface aminopeptidases, notably aminopeptidase B and leucine aminopeptidase. Activates macrophages and T lymphocytes. Has antitumor properties.	Methanol	1-10 µM
Cathepsin Inhibitor I	219415	Selectively inhibits cathepsin B (k_2/K_i = 6.9 x 10^3 M^{-1} sec^{-1}), cathepsin L (k_2/K_i = 3.1 x 10^5 M^{-1} sec^{-1}), cathepsin S (k_2/K_i = 6.6 x 10^4 M^{-1} sec^{-1}), and papain (k_2/K_i = 1.8 x 10^3 M^{-1} sec^{-1}).	DMSO, Ethanol	100-200 µM
E-64 Protease Inhibitor	324890	An irreversible cysteine protease inhibitor that has no action on cysteine residues in other proteins. Specific active site titrant.	H_2O, DMSO	1-10 µM
EDTA, Disodium Salt, Molecular Biology Grade	324503	A reversible metalloprotease inhibitor. A chelator that may interfere with other metal ion-dependent biological processes.	H_2O	1-10 mM
Elastatinal	324691	A competitive inhibitor of elastase (K_i = 240 nM).	H_2O, DMSO, Ethanol	0.5-2 µg/ml
EST	330005	A membrane-permeable calpain inhibitor.	Ethanol	20-50 µg/ml
GGACK	347436	An irreversible inhibitor of Urokinase (IC_{50} < 1 µM).	H_2O	1-10µM
Leupeptin, Hemisulfate	108975	A reversible inhibitor of trypsin-like proteases and cysteine proteases, including endoproteinase Lys-C, papain, cathepsin B, trypsin, kallikrein, and thrombin.	H_2O	10-100 µM
Pepstatin A	516481	A reversible inhibitor of aspartic protease. Inhibits cathepsin D, cathepsin G, pepsin, and renin.	DMSO, Methanol	~ 1 µM
o-Phenanthroline	516705	A metalloprotease inhibitor.	DMSO, Ethanol, H_2O	
Phosphoramidon, Disodium Salt	525276	A highly specific inhibitor of thermolysin. Also inhibits the conversion of big endothelin-1 to endothelin-1.	H_2O, DMSO, Methanol	1-10 µM

TLCK, HCl	616382	An irreversible inhibitor of trypsin-like serine proteases. Inactivates trypsin, specifically and irreversible. Does not have any significant inhibitory effect on chymotrypsin.	H_2O	10-100 µM
TPCK	616387	An irreversible inhibitor of chymotrypsin. Useful for inhibiting chymotrypsin activity in trypsin preparations.	Ethanol, Methanol	10-100 µM

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